(19) JAPANESE PATENT OFFICE

PATENT ABSTRACTS OF JAPAN

(11) Publication number: 06213888 A

(43) Date of publication of application: 05 . 08 . 94

(51) Int. Cl G01N 33/53
G01N 33/549

(21) Application number: 04361873

(22) Date of filing: 24 . 12 . 92

(71) Applicant: FUJI YAKUHIN KOGYO KK

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(54) IMMUNOLOGICAL DETERMINATION METHOD OF HUMAN 72-KDA GELATINASE/IV-TYPE COLLAGENASE

(57) Abstract:

PURPOSE: To determine human pro MMP-2 within a sample to be tested rapidly with high sensitivity and accuracy by using two types of monoclonal antibodies which specifically combines with human 72-kDa gelatinase/IV-type collagenase (human pro MMP-2).

CONSTITUTION: Two types of monoclonal antibodies which specifically combine with human pro-MMP-2 are used as carriers which combine with solid phase carriers or antibodies which give labeled substances, thus performing measurement immunologically by the sandwich method. Balls, microplates, sticks, fine particles, or test tubes made of for example polystyrene and polycarbonate for well adsorbing protein such as antibodies can be selected arbitrarily and used as the solid phase carriers. On the other hand, after an object containing antibodies is fractionated with ammonium sulfate as antibodies giving the labeled substance, anion exchange gel and IgG fraction are performed and further specifically combined part Fab' which is obtained by reduction after pepsin digestion can be used.

(19) JAPANESE PATENT OFFICE

PATENT ABSTRACTS OF JAPAN

(11) Publication number: 06300757 A

(43) Date of publication of application: 28 10 94

(51) Int. Cl G01N 33/53

(21) Application number: 05118909

(22) Date of filing: 12 . 04 . 93

(71) Applicant: FUJI YAKUHIN KOGYO KK

(72) Inventor: HAYAKAWA TARO
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SAKAI CHIE
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TOKAI HIDEAKI
NAGAI YASUO
YOSHIDA SHINICHI

(54) IMMUNOASSAY FOR COMPLEX OF HUMAN INTERSTITIAL COLLAGENASE AND INHIBITOR AND APPLICATION TO CLINICAL DIAGNOSIS

(57) Abstract:

PURPOSE: To determine a human active MMP-1-TIMP-1 complex in a sample material by using a monoclonal antibody which connects specifically with each of human MMP-1 and TIMP-1.

CONSTITUTION: A monoclonal antibody specifically bonding with human MMP-1 is prepared by using purified pro-MMP-1 as an immune source which is obtained by purifying human pro MMP-1 from a supernatant fluid of normal dermoblasts. The monoclonal antibody reacts specifically to the pro-MMP-1 and active MMP-1. For a solid carrier at the determination according to this immunoassay, a ball of polystyrene or the like well adsorbing protein such as the antibody, a test tube, etc., are optionally selected and used. Meanwhile, an antibody for labelling is an IgG fraction which is obtained by fractioning a substance including the antibody by ammonium sulfate and purifying with an anion exchanger, for instance, an enzyme, a chemical substance or the like. A human active MMP-1-TIMP-1 complex in the blood serum of a patient like a cancer patient who shows sthenia in the acitivity of collagenase is thus determined and the method is applied to diagnose a group of diseases.

(19) JAPANESE PATENT OFFICE

PATENT ABSTRACTS OF JAPAN

(11)Publication number: **07159402 A**

(43)Date of publication of application: **23. 06 . 95**

(51)Int. Cl **G01N 33/53**

(21)Application number: **05340357**

(22)Date of filing: **09 . 12 . 93**

(71)Applicant: **KYODO NYUGYO KK**

(72)Inventor: **TANI HISANORI**
HIRONAKA TAKAHIRO
NONOMURA KAZUHIKO

(54)IV TYPE COLLAGENASE MEASURING METHOD

(57)Abstract:

PURPOSE: To detect the content of MMP (metalloproteinase)-2 and MMP-9 in oncocytes procuring a metastasizing function or serum of a cancer patient by immobilizing an antibody to the MMP-2 or MMP-9 to be brought into contact with an ecological sample preparation liquid which may contain the MMP-2 or MMP-9.

CONSTITUTION: An antibody to MMP-2 (E.C. 3, 4, 24, 24) or MMP-9 (E.C. 3, 4, 24, 35) is immobilized on a sensor section of a BIA-core biosensor and is brought into contact with an ecological sample preparation liquid which may contain the anti-body and the MMP-2 or MMP-9 to measure the amount of the MMP-2 or MMP-9 bonded to the antibody by a surface plasmon resonance. Since there is a very high correlation between the activity of the MMP-2 or MMP-9 and the invasion or metastasis of oncocytes, and the content of the MMP-2 and -9 in the oncocytes procuring metastasizing function and serum of a cancer patient can be detected by an immunoassay using an antibody thereto, it is possible to be used for the inspection of the metastasis and malignancy of cancer.

(19) JAPANESE PATENT OFFICE

PATENT ABSTRACTS OF JAPAN

(11)Publication number: 08134098 A

(43)Date of publication of application: 28. 05 . 96

(51)Int. Cl C07K 16/18
C12N 5/10
C12P 21/08
G01N 33/53
G01N 33/577
// C12N 15/02
(C12P 21/08 C12R 1:91)

(21)Application number: 06301617

(22)Date of filing: 11 11 94

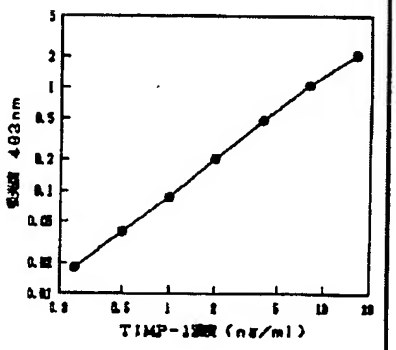
(71)Applicant: MORINAGA & CO LTD

(72)Inventor: KURODA KAZUHIKO
KATO MASATOSHI

(54)HIGH-SENSITIVITY MEASUREMENT OF HUMAN TIMP-1

(57)Abstract:

CONSTITUTION: TIMP-1 in a specimen is determined in high sensitivity through a sandwich enzyme immunoassay technique by using a labeled anti-human TIMP-1 mouse clonal antibody which reacts with human TIMP-1, but not with human TIMP-2 and bovine TIMP-1 under a reduced and a non-reduced conditions in the immunoblotting after SDS electrophoresis of human TIMP-1. This antibody is an IgG which does not inhibit the collagenase activity of the TIMP-1, and, when combining the labeled antibody with another antibody immobilized to an immunoplate



(19) JAPANESE PATENT OFFICE

PATENT ABSTRACTS OF JAPAN

11)Publication number: **08136548 A**

(43)Date of publication of application: **31. 05 . 96**

(51)Int. Cl **G01N 33/574**
G01N 33/493
G01N 33/573

(21)Application number: **06301616**

(22)Date of filing: **11 . 11 . 94**

(71)Applicant: **MORINAGA & CO LTD**

(72)Inventor: **KURODA KAZUHIKO**
KATO MASATOSHI

(54) **DIAGNOSTIC METHOD FOR URINARY ORGAN CANCER**

(57)Abstract:

PURPOSE: To diagnose urinary organ cancer easily by determining the tissue inhibitor of metalloproteinases (TIMP-1) in urine.

CONSTITUTION: Difference of the concentration of TIMP-1 in urine between a healthy person and a patient of urinary organ is conspicuous as compared with the difference of concentration of TIMP-1 in blood serum when a new monoclonal antibody for TIMP-1, obtained from human cell, is applied to enzyme immunoassay. Consequently, urinary organ cancer can be diagnosed easily without causing any pain to a subject by measuring the TIMP-1 in urine. The TIMP-1 in urine can be determined for bladder cancer, liver cancer and ren cancer. This method is preferably employed in immunoassay utilizing monoclonal antibody.

(19) JAPANESE PATENT OFFICE

PATENT ABSTRACTS OF JAPAN

(11) Publication number: 08217800 A

(43) Date of publication of application: 27 08 96

(51) Int. Cl C07K 16/40
C12N 15/02
C12P 21/08
G01N 33/53
G01N 33/573
G01N 33/577
//(C12P 21/08 , C12R 1:91

(21) Application number: 07050375

(22) Date of filing: 16 . 02 . 95

(71) Applicant: FUJI YAKUHIN KOGYO KK

(72) Inventor: OKADA YASUNORI
OUCHI EIKO
YAMAZAKI TOMOMI
TONO ISAO
YOSHIDA SHINICHI
IWATA KAZUSHI

(54) DETERMINATION OF HUMAN PROMATRIX METALLOPROTEASE-7 BY IMMUNOLOGICAL MEASURING METHOD

(57) Abstract:

PURPOSE: To provide a method for accurately determining or measuring and detecting promatrix metalloprotease 7 (MMP-7) useful for analyzing relationship between various diseases.

CONSTITUTION: This determination method comprises measuring human MMP-7, especially by sandwich enzyme immunoassay using a combined antibody comprising a monoclonal antibody capable of specifically recognizing the N-terminal region containing an amino acid sequence of R18-34 of pro-MMP derived from CaR-1 cell or the neighbor and a monoclonal antibody capable of specifically recognizing a C terminal region containing an amino acid sequence of R 253-267 as a measuring reagent. Furthermore, a reagent for measuring human MMP-7 by the method is provided. The reagent is capable of detecting, measuring an determining proMMP-7 found in cancer of the rectum and prostate cancer which are increasing at present as well as various cancer diseases. These monoclonal antibodies are further useful also as reagents for immunological dyeing of tissue and cell.

(19) JAPANESE PATENT OFFICE

PATENT ABSTRACTS OF JAPAN

(11) Publication number: 09023889 A2

(43) Date of publication of application: 28 01 97

(51) Int. Cl C12N 15/09 C07H 21/04 C12N 5/10 A61K 48/00

(21) Application number: 08181760

(22) Date of filing: 11 . 07 . 96

(30) Priority: 12 07 95 DE 19524720

(71) Applicant: HOECHST AG

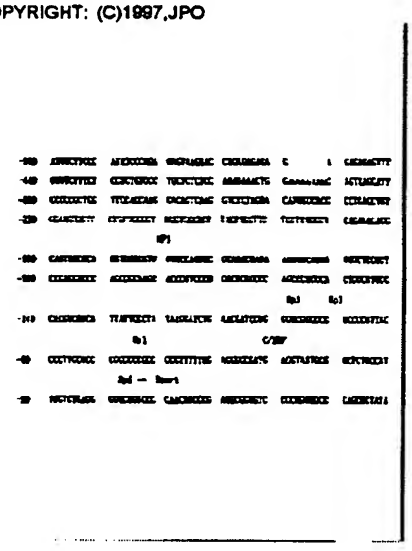
(72) Inventor: SEDLACEK HANS-HARALD DR
WICK MARISA
MUELLER ROLF

(54) CELL-SPECIFIC GENETIC THERAPY USING NEW PROMOTER FOR TISSUE INHIBITOR OF METALLOPROTEINASE-3

(57) Abstract:

PROBLEM TO BE SOLVED: To obtain a new promoter made up from a promoter-activating DNA fragment comprising a specific nucleotide sequence and effective for the gene of a metalloproteinase-3 tissue inhibitor used for a cell-specific genetic therapy, etc.

SOLUTION: This new promoter effective for the gene of a metalloproteinase-3 tissue inhibitor made up from a promoter-activating DNA fragment comprising the positions $^{2}463$ to $^{3}-2$ units of a nucleotide sequence of the formula. The new promoter is useful for a target cell-specific genetic therapy, a genetic diagnosis, etc. The promoter is obtained by isolating a genome DNA from a culture cell, WI-38 cell, making a gene library from the genome DNA by a conventional method, screening the library with a 30bp-long oligonucleotide obtained from the 5'-end region of the cDNA of the tissue inhibitor of the metalloproteinase-3, and subsequently treating the obtained DNA with a restriction enzyme.



(19) JAPANESE PATENT OFFICE

PATENT ABSTRACTS OF JAPAN

(11) Publication number: 09084589 A

(43) Date of publication of application: 31 . 03 97

(51) Int. Cl C12N 15/09
C07H 21/04
C12N 5/10
C12N 9/64
G01N 33/574
// A61K 38/46
C07K 16/40
C12P 21/08
(C12N 15/09 , C12R 1:91), (C12N 5/10 , C12R 1:91), (C12N 9/64 , C12R 1:91), (C12P 21/08 , C12R 1:91

(21) Application number: 08200984

(22) Date of filing: 12 . 07 . 96

(30) Priority: 14 . 07 . 95 JP 07200319

(71) Applicant: FUJI YAKUHIN KOGYO KK

(72) Inventor: SEIKI MOTOHARU
SATO HIROSHI

(54) NEW PROTEIN

(57) Abstract:

PROBLEM TO BE SOLVED: To obtain a new protein of a kind of a matrix metalloprotease(MMP) having an activating function against MMP-2, expressing specifically on the surface of a human tumor cell and useful for diagnosis and treatment of cancer, etc., such as a diagnosis of the presence of tumor cell and the grade of malignancy of tumor.

SOLUTION: This is a kind of a matrix metalloprotease(MMP) having an activating function against a latent-type MMP-2 which specifically expresses on the surface of a human tumor cell, and this new protein has the activity of the same level as a naturally occurring membrane-type MMP (MT-MMP) that is an activating factor against a latent-type MMP-2 beside MT-MMP-1. This protein is useful for a research relating to diagnosis and treatment of cancer, etc., such as a diagnosis of the presence of tumor cell and the grade of malignancy of tumor, and other medical and physiological uses, etc. The protein is obtained by isolating an mRNA from cells of human cancer of mouth, preparing a cDNA library using the mRNA, screening the library using a probe, integrating the obtained DNA into a vector and expressing the DNA in host cells.

(19) JAPANESE PATENT OFFICE

PATENT ABSTRACTS OF JAPAN

(11) Publication number: 09087299 A

(43) Date of publication of application: 31 . 03 97

(51) Int. Cl C07K 16/40
C07H 21/04
C12N 5/10
C12N 15/02
C12N 15/09
C12P 21/08
C12Q 1/68
G01N 33/574
G01N 33/577
// A61K 38/46
A61K 39/395
A61K 48/00
C12N 9/64
(C12N 5/10 , C12R 1:91), (C12P 21/08 , C12R 1:91)

(21) Application number: 08200985

(22) Date of filing: 12 . 07 . 96

(30) Priority: 14 . 07 . 95 JP 07200320

(71) Applicant: FUJI YAKUHIN KOGYO KK

(72) Inventor: SHINAGAWA AKIRA
SEIKI MOTOHARU
SATO HIROSHI

(54) MONOCLONAL ANTIBODY SPECIFIC TO MMP-2 ACTIVATION FACTOR

(57) Abstract:

PROBLEM TO BE SOLVED: To obtain a new antibody having specificity to a protein which is a kind of matrix metalloprotease (MMP) having the activity of a latent MMP-2, exhibiting an activity equivalent to the activity of natural membrane-type MMP and useful for the diagnosis of the presence of cancer cell and the grade of malignancy, etc.

SOLUTION: This new monoclonal antibody has specificity to a protein (salt) or its partial peptide (salt) having an activity equivalent to the activity of a natural matrix metalloprotease (MMP) which is a kind of MMP having the activating property on latent MMP-2 and a latent MMP-2 activation factor other than a membrane-type MMP-1 (MT-MMP-1). It is useful for the diagnosis and treatment for cancer such as the presence of cancer cell and the diagnosis of the degree of malignancy of the cancer and other medical and physiological uses. The antibody can be produced by immunizing a mouse with a recombinant MT-MMP-3, fusing the spleen cell of the mouse to a myeloma cell, culturing on a HAT medium, selecting an antibody-producing strain, cloning the strain by limiting dilution analysis and culturing the obtained hybridoma.

(19) JAPANESE PATENT OFFICE

PATENT ABSTRACTS OF JAPAN

(11) Publication number: 09136841 A

(43) Date of publication of application: 27 . 05 97

(51) Int. Cl A61K 45/00
C12N 9/99
// A61K 35/58
A61K 38/00
A61K 38/00
A61K 38/00
A61K 38/00
A61K 38/00
C07C237/22

(21) Application number: 08208490

(22) Date of filing: 07 . 08 . 96

(30) Priority: 07 . 08 . 95 IT 95RM 557

(71) Applicant: POLIFARMA SPA

(72) Inventor: POLITI VINCENZO
DALESSIO SILVANA
GIOVANNI DI STAZIO
GIOVANNA DE LUCA
MARIO MATERAZZI

(54) ASSAY OF EFFICACY IN TERMS OF THERAPY FOR METALLOPROTEINASE INHIBITOR, NEW INHIBITOR, AND ITS USE IN THERAPY

(57) Abstract:

PROBLEM TO BE SOLVED: To provide a method for quantitatively and highly reliably evaluating the activity of a substance inhibiting an enzyme existing in snake venom and mammal body, and to obtain the inhibitor evaluated by the method.

SOLUTION: (A) Using a zinc-dependent metalloproteinase existing in the venom of snakes belonging to Grotalidae or Viperidae, the inhibitory activity of a peptide analogue having ability to inhibit the above enzyme is subjected to primary screening. Subsequently, (B) the inhibitory activity of the above-mentioned peptide analogue against the zinc-dependent metalloproteinase existing in mammal body is assayed. Then, (C) the activity of the peptide analogue for a relevant morbid state is demonstrated by the standard pharmacological examination. The peptide analogue is e.g. a compound of formula I [A is a group of formula II; Y is OH, NH_2, NHOH, etc.; R4 is CH-$(CH_3)_2$, phenyl, etc.; X is 5-methoxy-1-indanon-3-acetyl, naphthoyl, etc.].

X-A-Cyt-Y
|
R4 I

NH-CH-CO
/
CH2- II

(19) JAPANESE PATENT OFFICE

PATENT ABSTRACTS OF JAPAN

(11) Publication number: 09206099 A

(43) Date of publication of application: 12 . 08 . 97

(51) Int. Cl C12Q 1/28
G01N 33/48

(21) Application number: 08015268

(22) Date of filing: 31 . 01 . 96

(71) Applicant: SEKISUI CHEM CO LTD

(72) Inventor: KOBAYASHI KOJI
KURIYAMA KIYOSHI

(54) CELL FUNCTION ASSAY

(57) Abstract:

PROBLEM TO BE SOLVED: To provide a new method for assaying cell function by assaying productivity of myeloperoxidase or matrix metalloproteinase in a further simplified assay system by using whole blood.

SOLUTION: Blood is brought into contact with a material having such uneven surface as to be 0.2-10$_{\mu}$m in centerline average roughness Ra value and 5-20$_{\mu}$m in unevenness average spacing Sm value to induce production of myeloperoxidase (or matrix metalloproteinase), thus assaying the production of the enzyme.

(19) JAPANESE PATENT OFFICE

PATENT ABSTRACTS OF JAPAN

(11) Publication number: 10210982 A

(43) Date of publication of application: 11 08 98

(51) Int. Cl C12N 15/09
C07K 14/47
C07K 16/40
C12N 1/21
C12N 5/10
C12N 9/00
C12N 9/48
C12N 15/02
C12P 21/02
C12P 21/08
G01N 33/53
//(C12N 1/21 , C12R 1:19), (C12P 21/02 , C12R 1:91)

(21) Application number: 09031505

(22) Date of filing: 31 . 01 . 97

(71) Applicant: FUJI YAKUHIN KOGYO KK

(72) Inventor: SEIKI MOTOHARU
SATO HIROSHI
AOKI TAKANORI
YOSHIDA SHINICHI

(54) NEW PROTEIN

(57) Abstract:

PROBLEM TO BE SOLVED: To obtain a new protein, which is one kind of matrix metalloproteinase(MMP), having an ability to activate a latent type gelatinse A and natural murine MT-MMP activities and useful for diagnosis, etc., of the presence or absence of cancer cells and the malignancy of cancers.

SOLUTION: This new protein is a new protein (salt) derived from a mouse which is one kind of matrix metalloproteinase(MMP) having an ability to activate a latent type gelatinase A and activities of natural murine MT-MMP which is a latent type gelatinase A activating factor other than murine MT 1-MMP or activities substantially equal thereto. The protein is useful for diagnosis, treatment, etc., of cancers such as diagnosis, etc., of the malignancy of the cancers. Furthermore, the protein is obtained by screening a murine pulmonary cDNA library with a human MT1-MMP cDNA fragment as a probe, integrating the resultant gene into a vector, transferring the resultant gene into a host cell such as Escherichia coli and expressing the gene.

(19) JAPANESE PATENT OFFICE

PATENT ABSTRACTS OF JAPAN

(11)Publication number: **10287700 A**

(43)Date of publication of application: **27. 10 . 98**

(51)Int. Cl **C07K 16/40**
C12N 5/10
G01N 33/53
G01N 33/573
G01N 33/577
// C12N 15/02
C12P 21/08
(C12N 5/10 C12R 1:91),
(C12P 21/08 C12R 1:91

(21)Application number: **09106846**

(22)Date of filing: **10 . 04 . 97**

(71)Applicant: **FUJI YAKUHIN KOGYO KK**

(72)Inventor: **OKADA YASUNORI**
TONO ISAO
FUJIMOTO NOBORU
TEJIMA YOSHINORI
YOSHIDA SHINICHI
IWATA KAZUSHI

(54)**ANTIBODY AGAINST ACTIVE TYPE MATRILYSIN (MMP-7) AND IMMUNOASSAY USING THE SAME**

(57)Abstract

PROBLEM TO BE SOLVED: To provide an accurate method for quantitatively determining or measuring an active type matrix metalloprotease 7 (MMP-7) useful for analyzing the relation of a matrilysin called a human MMP-7 which is one of the matrix metalloproteases with various diseases.

SOLUTION: The monoclonal antibody capable of specifically carrying out the immunological reaction only with a human active type MMP-7 is obtained according to a cell fusion method by using an amino acid sequence of YSLFP of the MMP-7 or a region containing the vicinity thereof as an immunogen. The resultant antibody is used as a measuring reagent to provide a method for especially sandwich enzyme immunologically performing measurements of the human active type MMP-7 and a reagent therefor. The method and reagent are capable of detecting, measuring and determining the active type MMP-7 found in various cancer diseases including rectal cancer and prostatic cancer which are presently increasing. The monoclonal antibody is further useful as a reagent for immunological staining of tissues or cells.